THE UNIVERSITY OF TEXAS
MD ANDERSON
CANCER CENTER

September 22, 1999

Philip J. Migliore, M.D.
Research Director, The Moran Foundation
Department of Pathology
Baylor College of Medicine
One Baylor Plaza
Houston, Texas 77030

Dear Dr. Migliore:

Per your request, I am sending you a progress report of my Moran Foundation project (98-0100). A portion of this work was presented as a platform presentation at the 1999 United States and Canadian Academy of Pathology Annual Meeting in San Francisco, California. The title of this talk was "Retinoblastoma Protein in Colonic Aberrant Crypt Foci and Adenocarcinoma." I have also submitted the manuscript, "Increased Expression of the Retinoblastoma Protein in Colonic Adenomas and Adenocarcinomas" to *Archives of Pathology & Laboratory Medicine*. This manuscript is currently being reviewed. I anticipate that a second manuscript detailing this work will be completed within 6 months. Most of this project is completed, but there are some experiments that are still in progress (please see attached progress report for details).

I would like to thank you and the Moran Foundation committee for your support with this research project. If you have any further questions, please call me at office (713) 745-2794 or beeper (713) 404-6380.

Sincerely,

Russell Broaddus, M.D., Ph.D.
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Progress Report – Moran Foundation Project 98-0100

Specific Aim 1: Isolate ACF from the flat mucosa of human colectomy surgical specimens containing colon carcinoma.

Approximately 70 aberrant crypt foci (ACF) were successfully isolated from colectomy specimens from Ben Taub General Hospital. These ACF were characterized by light microscopy as hyperplastic, dyplastic, or indeterminate.

Specific Aim 2: Characterize pRb expression immunohistochemically in ACF

Our preliminary results with Rb immunohistochemistry suggest that the Rb protein is over-expressed in the apical portion of dysplastic ACF, but only faintly expressed in the basal portion of hyperplastic ACF. We have stained a few of the indeterminate ACF and have found that a sub-set shows increased apical Rb expression as in the dysplastic ACF. Thus, increased apical expression of Rb may be an early marker for dysplasia. We are currently staining the remainder of the ACF in our collection.

Specific Aim 3: Determine the relationship of the ACF proliferative cell compartment with pRb expression.

We have stained some of the ACF with Ki-67. The hyperplastic ACF show Ki-67 staining in the basal portion of the crypts, while the dysplastic ACF have increased staining in the apical portions of the dysplastic crypts. Therefore, the preliminary results suggest that the Rb-positive cell compartment of the ACF is the proliferative compartment. We have not yet performed dual Rb/DNA flow cytometry of small adenomas.

Specific Aim 4: Determine Rb gene copy number in ACF by Fluorescent <u>in</u> <u>situ</u> Hybridization

These experiments are still in progress. We have started these experiments by first using colonic adenocarcinomas that immunohistochemically over-express Rb. Our initial pilot studies have failed to demonstrate any hybridization in the tumors. We are currently trying different tissue digestion procedures in order to optimize hybridization conditions.